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First-in-Human Studies: Global Regulatory and Translational Considerations

Moscone North, Room 135

Wednesday, October 30, 2013, 8:00 AM–11:48 AM

Abstract nos: 122-126

TCT-122

Electrode irrigation alters RF ablation treatment zone geometry and preserves medial and adventitial tissue while maintaining injury to renal nerves

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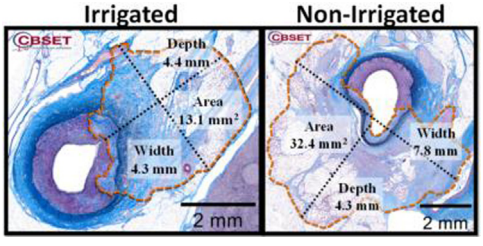
Background: We quantitatively compared lesion geometry and artery and nerve injury with and without irrigation during RF ablation to enable optimization of catheter design and understanding of temperature gradients.
Methods: RF ablations, using spatially discrete electrodes, were conducted in swine using THERMOCOOL® irrigated tip catheter (Biosense Webster, CA) with and without irrigation. Arteries were harvested at 7d and serial sectioned every 300 µm and quantified histomorphometrically (Fig 1).



Results: Surface irrigation lowered affected luminal circumference (irrigated 6.1% vs. non-irrigated 44.6%); media (irrigated 11.7% vs. non-irrigated 35.4%); and EEL circumference (irrigated 18.9% vs. non-irrigated 45.4%). RF ablation effects in the nerve-rich adventitia were less sensitive to irrigation: width (irrigated 3.8mm vs. non-irrigated 4.8mm) and depth (irrigated 5.1mm vs. non-irrigated 3.4mm). Morphologic nerve changes within the ablation zones were comparable with and without irrigation and were considered to be marked and necrotic/degenerative.
Conclusions: Irrigation preserved arterial integrity and reduced linear, circumferential, and radial injury at the luminal surface and within media and adventitia while providing comparable nerve injury. These data were used to develop a computational model of RF energy delivery and injury for further optimization of irrigation and powering protocols.

TCT-123

Preliminary safety and efficacy results from the REALISE trial: REnAL denervatIon by ultraSound transcatheter Emission

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Background: Catheter-based renal denervation has emerged as a method for treating the overactivity of the sympathetic nervous system. The PARADISE system (ReCor Medical, Menlo Park, CA) is a unique therapeutic non-focused ultrasound system designed to perform circumferential renal denervation while preventing damage to the renal artery. The purpose of the REALISE trial is to evaluate the safety and efficacy of the PARADISE system in patients suffering from resistant hypertension.
Methods: The REALISE trial is a 20-patient prospective study conducted by multi-disciplinary teams at two sites in France (Hôpital Pitié-Salpêtrière, Paris; Hôpital Rangueil, Toulouse). Patients suffering from resistant hypertension as defined by the ESH-ESC guidelines (office blood pressure above 140/90 mmHg with a minimum of 3 antihypertensive drugs including a diuretic) were screened and eligibility further confirmed by home and/or ambulatory measurements. Renal denervation was performed bilaterally with the PARADISE system, delivering 2 to 3 ultrasound emissions in each artery. All patients underwent CT-scan or MRI at baseline and follow-up to assess the renal arteries.
Results: Preliminary results indicated that 63% of enrolled and treated patients were under spironolactone therapy. Bilateral denervation was performed by delivering an average of 5.7 ultrasound emissions in each subject (average heating time 3.3 minutes per subject). Sedatives and analgesics were administered during the intervention and the treatment was well tolerated by all patients. Preliminary results at 6 months were comparable to published data on radiofrequency renal denervation with an average reduction in office and ambulatory blood pressure of -21/-9 mmHg and 9/ 4 mmHg, respectively. Systematic imaging of the renal arteries showed no arterial stenosis or arterial damage at follow-up.
Conclusions: Endovascular ultrasound renal denervation appears to be a safe and effective treatment for resistant hypertension. Results on all 20 patients from the REALISE study will be presented at the conference.

TCT-124

A novel appliance for transcatheter mitral cerclage annuloplasty

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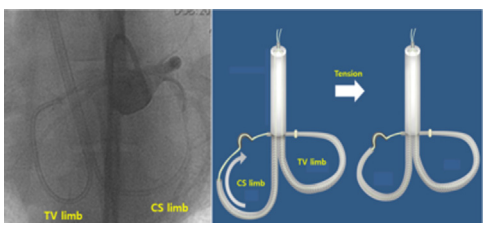
Background: Mitral cerclage annuloplasty is a transcatheter coronary sinus annuloplasty that establishes circumferential tension around the mitral annulus by traversing the basal interventricular septum between the great cardiac vein and the right ventricular outflow tract. We have developed a novel implant to effect annuloplasty while preventing myocardial erosion; avoiding compression of coronary arteries, tricuspid leaflet, AV node; and displaceing the knot fixation to a safe caval location.
Methods: The cerclage appliance is positioned over a 0.018" nylon-coated flexible and radiopaque stainless steel braidwire. It consists of conjoined semirigid coronary sinus and trans-tricuspid limbs (CS, TV, Figure) and is used along with a coronary artery protection arch. X-ray guided cerclage was performed in swine (n=6, 55～80kg) to investigate the device performance.
Results: The cerclage appliance was easily delivered over the cerclage suture and assumed its intended anatomic position along the coronary sinus and across the tricuspid valve. Tension accomplished circumferential mitral annular reduction while the TV limb protected the TV and AV node from direct contact. Neither conduction block nor TV malfunction was observed after two-week survival (n=1).
Conclusions: This novel cerclage appliance addresses potential shortcomings of transcatheter cerclage annuloplasty in a simple-to-deploy device.



TCT-125

Novel Thoracoscopically Assisted Trans-Catheter Ventricular Restoration Therapy: Feasibility and Efficacy in an Anteroseptal Aneurysmal Ovine Model

Yanping Cheng[1], Geng-Hua Yi[1], Lon S. Annest[2], Kevin Van Bladel[2], Masahiko Shibuya[1], Carlos A. Gongora[1], Gerard B. Conditt[1], Armando Tellez[1], David Schickling[2], Andrew Boyle[3], Ryan A. Brown[4], Vasco G. Ribeiro[5], Greg L. Kaluza[1], Juan Granada[1]
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Background: Surgical ventricular reconstruction has been used as heart failure treatment in patients with large ventricular aneurysms. Based on a well-established device-based (BioVentrix, San Ramon, CA) surgical technique operation, this study assessed the feasibility of performing minimally invasive thoracoscopically assisted transcatheter ventricular restoration (TCVR) in an anteroseptal ovine infarction model.
Methods: Ventricular aneurysmal model development was achieved by coil-occlusion of the left anterior descending artery. 8 weeks after occlusion, TCVR was performed in five sheep via a 4 cm left thoracotomy. Under endoscopic and fluoroscopic guidance, LV scar was visualized and trans-epicardial puncture was performed advancing a guidewire at the lateral margin of the scar, across a portion of the LV, and through the interventricular septum into the right ventricle. With one end still protruding from the left chest, the guidewire was retrieved with a snare via the right external jugular vein through a percutaneous approach. Then an inner anchor on a tether was inserted over the wire and positioned on the right side of the interventricular septum. The opposite end of the tether protruded through LV anterolateral wall and an outer locking anchor was deployed over the tether on the LV anterior epicardium. Serial pairs of anchors were then approximated to exclude the intervening portion of the

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wall. LV performance was evaluated before (baseline) and immediately after device implantation by echo.
Results: TCVR was successfully performed in all the animals. Immediately after the procedure and compared to baseline, LV end-systolic volume was decreased by 54% (26.9±8.7 vs. baseline 60.1±22.2ml, p<0.01) and end-diastolic volume decreased by 34% (54.5±11.0 vs. baseline 85.6±20.6ml, p<0.05). Ejection fraction was significantly increased by 19.8% (51±9% vs. baseline 31±9%, p<0.001) and stroke volume was preserved (27.5±6.9 vs. baseline 25.5±3.8ml, p=NS).
Conclusions: Minimally invasive thoracoscopically assisted TCVR is feasible and resulted in significant improvement in cardiac volume and ejection fraction in an ovine infarction model.

TCT-126

First-in-human experience with a novel high-flow percutaneous heart pump

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Background: High-risk percutaneous coronary interventions (HRPCI) involving complex disease and/or depressed cardiac function have become increasingly common. The potential benefit from short-term mechanical circulatory support is suggested by observations that intraprocedural hemodynamic compromise may impact completeness of revascularization and contribute to adverse events. We report outcomes from a First in Human trial using the HeartMate PHP™ (Percutaneous Heart Pump) in patients undergoing HRPCI.PHP is a catheter-based axial flow pump designed to provide partial left ventricular support of up to 5 lpm and is rapidly delivered percutaneously via typical femoral insertion. The 12F catheter contains a distal collapsible covered nitinol cannula with an integrated impeller that expands to 24F when deployed across the aortic valve.
Methods: 10 patients with complex coronary disease and reduced LV function (EF from 26% - 34% prior to PCI) underwent elective HRPCI while on PHP support. Device success, defined as the deployment, use and removal of PHP without device failure; and periprocedural measures of hemodynamics and cardiac performance were evaluated. Major adverse safety and efficacy events were assessed during PHP use and at 30 days.
Results: Among the first 3 patients, PHP was successfully deployed in all patients without complications. There was no periprocedural or follow-up echocardiographic evidence of aortic regurgitation or valve abnormalities. All patients remained hemodynamically stable while on support and all planned target lesions were revascularized. The PHP was successfully removed in all cases and there were no adverse patient events while on device support through 30 days. (Outcomes on the full patient series will be presented when complete.)

	CARDIAC INDEX		MAP		PCWP	
	Baseline	On Support	Baseline	On Support	Baseline	On Support
Pt #1	2.8	3.17	73	65	41	16
Pt #2	2.67	2.45	84	112	11	5
Pt #3	2.3	3.26	97	119	8	9

Conclusions: In a First in Human trial involving patients undergoing HRPCI, hemodynamic support using the HeartMate PHP is feasible and safe.

25 Years of Interventional Innovation: Novel Therapies and the "Emerging" Device Concepts for 2013

Moscone West, 3rd Floor, Room 3005-3007

Monday, October 28, 2013, 8:00 AM–6:35 PM

Abstract nos: 127-136

TCT-127

Trans-Auricular Intra-Pericardial Tricuspid Annuloplasty (TRAIPTA)

Toby Rogers[1], Kanishka Ratnayaka[1], William H. Schenke[1], Anthony Z. Faranesh[1], Merdim Sonmez[1], Dominique N. Franson[1], Robert J. Lederman[1]
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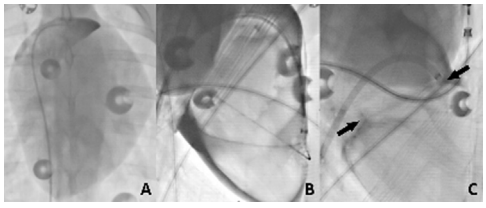
Background: Functional tricuspid regurgitation (TR) is clinically significant. TR predicts mortality independent of LVEF, age or pulmonary artery pressure. Persistent TR after mitral valve surgery is an independent poor prognostic sign. Tricuspid valve repair is usually an adjunct to other surgery. We present TRAIPTA, a novel percutaneous treatment of functional TR. We demonstrate pre-clinical feasibility in swine.
Methods: Through the femoral vein and under X-ray guidance, the pericardial space is accessed by puncture through the right atrial appendage (Panel A). A custom memory-shape delivery device positions a suture circumferentially in the AV groove (Panel B) and used to deploy a semi-rigid device to apply direct compression to the tricuspid annulus. The suture is tightened to achieve the desired degree of annuloplasty (Panel C), then secured and cut. The atrial appendage access is closed with an occluder.



Results: In naïve swine, trans-auricular pericardial access was easy and safe. The TRAIPTA device is consistently delivered to the AV groove, tension can be selectively applied to the tricuspid annulus, and RV geometry interactively altered.
Conclusions: Percutaneous treatment of functional TR is feasible in swine using TRAIPTA.

TCT-128

Transcatheter Implantation of Self-Expandable Vena Cava Valves for Treatment of Tricuspid Regurgitation: First-Human-Case Description

Hans R. Figulla[1], Torsten Doenst[2], Marcus Franz[2], Ali Hamadanchi[3], Daniel Kretzschmar[3], Alexander Lauten[2]
[1]Friedrich-Schiller Universitat, Jena, Germany, [2]University Hospital Jena, Jena, Germany, [3]Heart Center of the Friedrich-Schiller-University, Jena, Thuringia

Background: Despite the recent advances in interventional treatment of heart valve disease, no transcatheter approach is established for severe tricuspid regurgitation (TR). Single valve implantation into the inferior vena cava (IVC) has been suggested, which however only partially resolves the hemodynamic sequelae of TR. After extensive preclinical evaluation, we herein report the first human case of bi-caval self-expanding valve implantation (CAVI) in the superior (SVC) and inferior vena cava.
Methods: CAVI was performed in a 83-year-old patient with severe TR, chronic right heart failure and congestive hepatopathy. Two self-expanding pericardial valves were custom-made to fit to the anticipated implantation zones in the caval veins of this patient. Both devices were implanted under flouroscopy using a 27F-catheter and deployed at the level of the cavo-atrial junction of the SVC and the IVC. To protect the hepatic veins from backward flow, the inferior valve was aligned just above the hepatic vein inflow and deployed with the valve protruding into the right atrium (RA).
Results: After deployment and during 3-month follow-up excellent valve function was observed. The procedure resulted in a marked reduction of the pressure in the SVC and IVC from 27/14mmHg and 28/15mmHg to 21/7mmHg and 13/6mmHg at 3 month, respectively. After implantation symptoms of right heart failure resolved and did not recurr during follow-up and synthetic liver function recovered. The patients physical capacity improved with an increase in distance covered in 6-minute-walk-test from 20m before implantation to 200m at 3 month.
Conclusions: In this first-in-man experience, transcatheter CAVI proved feasible and resulted in persistent hemodynamic and clinical improvement. Further confirmatory experience with longer follow-up is required to evaluate the clinical benefit of the procedure.

TCT-129

Percutaneous Transfemoral Management of Severe Secondary Tricuspid Regurgitation with Edwards Sapien XT Bioprosthesis in patients with severe heart failure: first in man experience

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[1]Charité University Hospital, berlin, Berlin, [2]Charite, Berlin, Berlin, [3]Charité, Berlin, Berlin, [4]Charité - Campus Mitte, Berlin, Germany

Background: Severe tricuspid regurgitation (STR) is a common final pathway in advanced stages of heart failure (HF) and associated with increased morbidity and mortality. The prevalence of moderate to severe TR is 35% in HF patients occurring in 1.6 Mio patients in the US. In advanced TR stages, the surgical risk is prohibitively high, alternative approaches are therefore required. Here we describe the feasibility as well as periprocedural and short-term outcomes of a novel first-in-man single caval and dual caval approach for implantation of the Edwards Sapien XT.
Methods: Vena cava inferior (VCI) single valve approach: to guarantee stable placement we prepared a landing zone by implanting a self-expanding 30/60-mm Sinus XL Stent in the IVC segment downstream of the RA. To further downsize the